General

Guideline Title

Care of the HIV-exposed infant with indeterminate status.

Bibliographic Source(s)

New York State Department of Health. Care of the HIV-exposed infant with indeterminate status. New York (NY): New York State Department of Health; 2014 Jan. 15 p. [28 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The quality of evidence (I-III) and strength of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Important Notes

The recommended routine postnatal prophylaxis for all human immunodeficiency virus (HIV)-exposed infants has changed. The new recommended dosing is as follows:

- Zidovudine (ZDV) syrup, 4 mg/kg per dose PO given twice daily through 6 weeks of age, started as soon as possible (within 6 hours, and no later than 12 hours of delivery). See table below for dosing for premature infants <35 weeks' gestation.

Clinical scenarios that warrant supplemental prophylaxis are as follows:

- Mother received no antepartum therapy and only intrapartum ZDV
- Mother received no antepartum and no intrapartum prophylaxis
- Mother received antepartum therapy with incomplete (HIV ribonucleic acid [RNA] >1,000 copies/mL) or unknown degree of viral suppression
- Mother has known drug-resistant HIV

The recommended supplemental postnatal prophylaxis is as follows:

- ZDV as above

plus

- Nevirapine (NVP) – 3 doses given in the first week of life (see table below):
  - 12 mg PO per dose if BW >2 kg
  - 8 mg PO per dose if BW 1.5–2 kg

When treating infants born to mothers with known or suspected drug resistance, clinicians should consult with a pediatric provider who has experience with HIV treatment and management. Whenever possible, consultation should occur *before* delivery.

General Recommendations

All human immunodeficiency virus (HIV) infection-exposed infants should receive care from, or in consultation with, a pediatrician experienced with HIV treatment and management. (AI)

Newborn Antiretroviral (ARV) Prophylaxis for HIV-exposed Infants

Clinicians should administer zidovudine (ZDV) for prevention of mother-to-child-transmission of HIV to all HIV-exposed infants as soon as possible after birth (AI):

- ZDV (4 mg/kg PO twice daily) should be administered as soon as possible after birth, within 6 hours, and no later than 12 hours of delivery (AII)
- ZDV prophylaxis should be given for 6 weeks (AI); dose adjustments should be made as the infant's weight changes
- Dosing of ZDV prophylaxis should be adjusted for premature infants <35 weeks' gestational age (see table below) (AII)

Clinicians should administer supplemental ARV prophylaxis as close to the time of birth as possible for the following infants:

- Infants born to HIV-infected women who received no antepartum antiretroviral therapy (ART) and only intrapartum ZDV
- Infants born to HIV-infected women who received no antepartum ART and no intrapartum ZDV
- Infants born to HIV-infected women with suboptimal viral load levels (>1,000 copies/mL) (*consider*)
- Infants born to HIV-infected women with known drug-resistant HIV.

The preferred prophylactic regimen includes 6 weeks of daily ZDV *plus* 3 doses of nevirapine (NVP) administered during the first week of life (at birth, 48 hours after the first dose, and 96 hours after the second dose). See table below for dosing. (AI)

Clinicians should consult a pediatric provider who has experience with HIV treatment and management when using combination regimens other than those shown in Table 1 below and should discuss potential risks and benefits with the mother. Whenever possible, consultation should occur *before* delivery. At each visit, clinicians should:

- Educate and demonstrate to the caregiver how to measure and administer the correct ZDV dosage to be given to the infant because the dosage will change as the infant's weight changes
- Recommend and provide infant oral syringes for administering accurate ZDV dosages
- Use vocabulary that caregivers can understand, regardless of educational level, and provide written information that is well organized and easy to understand
- Document in the medical record that administration of the accurate ZDV dosage was discussed with the caregiver

Key Point:

Birth facilities should routinely stock liquid formulations of ZDV and NVP for immediate use in infants born to HIV-infected mothers, as indicated in table below.

Table: Antiretroviral Prophylaxis Regimens to Reduce Mother-to-Child HIV Transmission in HIV-exposed Infants

Routine Postnatal Prophylaxis for All HIV-exposed Infants
Full-term Newborn Regimen (≥35 weeks' gestation) Start as soon as possible (within 6 hours, and no later than 12 hours of delivery)

- ZDV syrup, 4 mg/kg per dose PO given twice daily through 6 weeks of age[a]

Routine Postnatal Prophylaxis for All HIV-exposed Infants

Preterm Newborn Regimen
Start as soon as possible (within 6 hours, and no later than 12 hours of delivery)

- *For ≥30 to <35 weeks' gestation*: ZDV 2 mg/kg per dose PO [or 1.5 mg/kg per dose IV] given every 12 hours, then advance to 3 mg/kg/dose (2.3 mg/kg/dose IV) every 12 hours beginning at age 15 days through 6 weeks of age
- *For <30 weeks' gestation*: ZDV 2 mg/kg per dose PO [or 1.5 mg/kg per dose IV] given every 12 hours, then advance to 3 mg/kg/dose (2.3 mg/kg/dose IV) every 12 hours beginning at 4 weeks of age through 6 weeks of age

Supplemental Postnatal Antiretroviral Prophylaxis
(see Table 2 in the original guideline document for infants who should receive supplemental prophylaxis)

Drugs for Infant	Dosing	Duration
2-drug regimen: ZDV + NVP[b]	ZDV: *as above* (4 mg/kg per dose PO twice a day) NVP: 12 mg PO per dose if BW>2kg 8 mg PO per dose if BW 1.5-2 kg	Birth through 6 weeks 3 doses in first week of life: • 1st dose within first 48 hr of birth • 2nd dose 48 hr after 1st dose • 3rd dose 96 hr after 2nd dose

NVP, nevirapine; HIV, human immunodeficiency virus; IV, intravenous; ZDV, zidovudine.

[a]If unable to tolerate orally, administer ZDV 3.0 mg/kg per dose IV every 12 hours, started as soon as possible after birth (within 6 hours, and no later than 12 hours of delivery).

[b]Consultation with a pediatric provider who has experience with HIV treatment and management is advised before administering NVP to neonates who are <1.5 kg or <32 weeks estimated gestational age at birth.

Newborn Antiretroviral Prophylaxis: Specific Scenarios

Infants Born to Mothers Who Received Antepartum Antiretroviral Therapy with Undetectable HIV Viral Load Levels at Delivery

All infants whose mothers received antepartum ART with undetectable HIV viral load levels at the time of delivery should be given ZDV for 6 weeks (see table above). (AI)

Infants Born to Mothers Who Received Only Intrapartum Prophylaxis

Infants born to mothers who received only intrapartum ARV drugs should be given ZDV for 6 weeks *plus* 3 doses of NVP in the first week of life (see table above). (AI)

Infants Born to Mothers Who Did Not Receive Antepartum or Intrapartum Antiretroviral Drugs

All infants whose mothers did not receive antepartum ART or intrapartum ZDV should be given ZDV for 6 weeks plus 3 doses of NVP in the first week of life (see table above). (AI)

Infants Born to Mothers Who Have Received Antepartum/Intrapartum Antiretroviral Drugs but Have Suboptimal Viral Suppression Near Delivery

Providers should consult with a pediatric provider who has experience with HIV treatment and management of HIV-exposed infants to determine whether to use the two-drug regimen of ZDV + NVP (see table above) for infants of mothers with suboptimal viral suppression. (BIII)

Infants Born to Mothers with Antiretroviral Drug-Resistant Virus

Before delivery, clinicians should consult a pediatric provider who has experience with HIV treatment and management when treating infants born to mothers with known or suspected drug resistance. (BIII)

Antiretroviral Drug Dosing for Premature Infants

Use of ARV drugs other than ZDV and NVP should be avoided in premature infants (see table above). (BIII)

Clinicians should consult a pediatric provider who has experience with HIV treatment and management to determine the optimal regimen when the neonate is at high risk for HIV infection. (BIII)

Clinicians should consult with a pediatric provider who has experience with HIV treatment and management before administering NVP to neonates who are <1.5 kg or <32 weeks' estimated gestational age at birth.

Diagnostic Testing

New York State Department of Health (NYSDOH) recommends that all New York State (NYS) birth facilities and pediatricians caring for HIV-exposed infants use the Pediatric HIV Testing Services at the Wadsworth Center.

In New York State, HIV qualitative ribonucleic acid (RNA) testing (nucleic acid test or NAT) is recommended for early detection of HIV infection in infants. Testing should be performed at the following ages: (AII)

- Within 48 hours of birth (BIII)
- At 2 weeks of age (AII)
- At 4 to 6 weeks of age (AII)
- At 4 to 6 months of age (AII)

Positive HIV NAT results at any age should be confirmed by repeat testing as soon as possible on a new sample. (AII) Two independent positive test results definitively diagnose pediatric HIV infection in HIV-exposed infants and subsequent testing is not necessary.

Once a positive HIV test result is confirmed, the clinician should:

- Consult a provider with experience in pediatric HIV care (AI)
- Discontinue perinatal prophylactic ZDV, if still being administered (AI)
- Evaluate for initiation of combination ART as soon as possible (AI)

Two negative HIV NAT results, one obtained ≥4 weeks of age and one obtained ≥4 months of age, definitively exclude pediatric HIV infection in HIV-exposed infants. (AII)

Pneumocystis Jirovecii Pneumonia (PCP) Prophylaxis

Clinicians should initiate prophylaxis against PCP at 6 weeks of age for all HIV-exposed infants unless HIV diagnostic testing definitively or presumptively excludes HIV infection (see Table 3 in the original guideline document). Prophylaxis should be continued until the diagnosis of HIV infection is presumptively or definitively excluded (see definitions of exclusion below). (AII)

Feeding HIV-exposed Infants

In New York State, breastfeeding by HIV-infected women is contraindicated, even when the mother is receiving combination ART. (AI)

Clinicians should strongly advise breastfeeding mothers with newly suspected or diagnosed HIV infection to discontinue breastfeeding immediately. Clinicians should consult with a pediatric provider who has experience with HIV treatment and management to determine whether prophylaxis should be given to the infant.

Clinicians should advise HIV-infected women to avoid premasticating food for infants. (AII)

Immunizations

Clinicians should follow the Centers for Disease Control and Prevention (CDC) recommended immunization schedules for HIV-exposed and HIV-infected infants.

Frequency of Visits and Long-Term Follow-Up

All HIV-exposed infants should receive care from, or in consultation with, a pediatrician experienced with HIV treatment and management by at least 2 weeks of age, and again at 1 month, 2 months, 4 months, and 6 months.

Clinicians should evaluate for potential mitochondrial dysfunction in ARV-exposed children who develop significant organ system abnormalities. (BIII)

Clinicians should:

- Document *in utero* exposure to ARV drugs in the patient's permanent medical record (AIII)
- Report cases of prenatal exposure to ARV drugs to the Antiretroviral Pregnancy Registry

Definitions:

Quality of Evidence for Recommendations

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Human immunodeficiency virus (HIV) infection

Guideline Category

Counseling

Diagnosis

Prevention

Screening

Clinical Specialty

Allergy and Immunology

Family Practice

Infectious Diseases

Internal Medicine

Obstetrics and Gynecology

Pediatrics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

Substance Use Disorders Treatment Providers

Guideline Objective(s)

To provide guidance for the care of human immunodeficiency virus (HIV)-exposed infants with indeterminate status

Target Population

Infants at risk for developing human immunodeficiency virus (HIV) infection

Interventions and Practices Considered

1. Zidovudine (ZDV) for all human immunodeficiency virus (HIV)-exposed infants
2. Supplemental antiretroviral (ARV) prophylaxis
3. Consultation with pediatric provider
    - Education and demonstration of correct ZDV dosage
    - Provision of infant oral syringes
    - Documentation in medical record
4. Two-drug regimen of ZDV + nevirapine (NVP)
5. HIV qualitative ribonucleic acid (RNA) testing (nucleic acid test [NAT])
6. *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis
7. Advising against breast-feeding or premastication of food
8. Immunization
9. Follow-up care
    - Evaluation for potential mitochondrial dysfunction
    - Documenting and reporting exposure to ARV drugs

Major Outcomes Considered

- Mother-to-child transmission of human immunodeficiency virus (HIV)
- Drug resistant HIV
- *Pneumocystis jirovecii* pneumonia (PCP)
- Infant anemia

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The National Library of Medicine, PubMed Central, Cochrane library, and Medline databases were searched for the time frame: 1992-2013 (November 2013); most were from 2008 to 2013; very early studies (1992-1999) were cited for historical reasons.

The inclusion criteria used in the searches were: infants born to HIV-infected mothers; specific scenarios for infants born to HIV-infected mothers; maternal receipt of ART; premature infants. The specific search terms used were: HIV-infected infant; infant ARV prophylaxis; mother-to-child

HIV transmission; HIV-infected pregnant women; intrapartum ZDV; HIV RNA viral load; pneumocystis jirovecii pneumonia (PCP); breastfeeding; infant HIV diagnostic testing; infant anemia.

The literature was identified by the author of the draft guideline, and by the co-chairs of the committee in conjunction with program staff. All members of the committee submitted relevant literature to program staff and the author for review for the guideline revision.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence for Recommendation

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with HIV infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

*Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Guidelines Committee

- Committee for the Care of Women with HIV Infection
- Committee for the Care of Substance Users with HIV Infection
- Physician's Prevention Advisory Committee
- Pharmacy Advisory Committee

The Perinatal Committee, composed of Pediatricians and Obstetrician-Gynecologists, determined that a guideline was needed that would address care of infants born to mothers with human immunodeficiency virus (HIV) infection. One expert clinician authored the guideline. The committee reviewed the guideline draft and made recommendations to it. The committee convened on August 27, 2012 and May 20, 2013 by conference calls.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

The guideline draft is peer reviewed by 2 experts outside of the committee; the author incorporates any comments from the peer reviewers and the guideline is again reviewed by the Committee. Once the revision is accepted by the committee, the guideline was reviewed by an internal New York State approval process. Any recommended changes are discussed with the author and the Committee to reach consensus, if needed.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate care of human immunodeficiency virus (HIV)-exposed infants with indeterminate status

Potential Harms

- Toxicities from nevirapine (NVP) in the infant are rare but have included severe and potentially life-threatening rash and hepatic toxicity. Toxicities are much more common with NVP dosing for chronic infection than with the three-dose prophylactic regimen recommended for some neonates. For infants who receive NVP as prophylaxis but still become infected, resistance to NVP can occur.
- Anemia has been associated with the use of zidovudine (ZDV); therefore, some experts recommend obtaining a complete blood count (CBC) and differential prior to initiating ZDV.

Contraindications

Contraindications

- In New York State, breastfeeding by human immunodeficiency virus (HIV)-infected women is contraindicated, even when the mother is receiving combination antiretroviral therapy (ART)
- The use of lopinavir-ritonavir in infants under 2 weeks of age is contraindicated due to toxicity

Qualifying Statements

Qualifying Statements

When formulating guidelines for a disease as complex and fluid as human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), it is impossible to anticipate every scenario. It is expected that in specific situations, there will be valid exceptions to the approaches offered in these guidelines and sound reason to deviate from the recommendations provided within.

Implementation of the Guideline

Description of Implementation Strategy

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with human immunodeficiency virus (HIV) infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers, and consumers through mass mailings and numerous AIDS Institute-sponsored educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative (CEI), the AIDS Educational Training Centers (AETC), and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the New York State Department of Health (NYSDOH) Distribution Center.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the CEI and the AETC. The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

New York State Department of Health. Care of the HIV-exposed infant with indeterminate status. New York (NY): New York State Department of Health; 2014 Jan. 15 p. [28 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Jan

Guideline Developer(s)

New York State Department of Health - State/Local Government Agency [U.S.]

Source(s) of Funding

New York State Department of Health

Guideline Committee

Perinatal Transmission Committee

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

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